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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,082	08/07/2001	Lawrence J. Marnett	11672N/020868	1831
32885 7590 11/13/2008 STITES & HARBISON PLLC 401 COMMERCE STREET SUITE 800 NASHVILLE, TN 37219			EXAMINER PAK, YONG D	
			ART UNIT 1652	PAPER NUMBER
			MAIL DATE 11/13/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/924,082

Applicant(s)

MARNETT ET AL.

Examiner

YONG D. PAK

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6, 7, 9-43, 49-59, 61 and 62 is/are pending in the application.
- 4a) Of the above claim(s) 22-43 and 49-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-7, 9-21, 55-59, and 61-62 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 25, 2008, canceling claim 4 and amending claims 6 and 13 has been entered.

Claims 6-7, 9-43, 49-59 and 61-62 are pending. Claims 22-43 and 49-54 are withdrawn. Claims 6-7, 9-21, 55-59 and 61-62 are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on August 25, 2008, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objection

In view of the amendment of claim 6, the objection to claim 6 has been **withdrawn**.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In view of the cancellation of claim 4, the rejection of claim 4 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been **withdrawn**.

Claim Rejections - 35 USC § 102

In view of the cancellation of claim 4, the rejection as being anticipated by Yu et al. under 35 USC 102(b) has been **withdrawn**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-7, 9-21 and 55-62 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. in view of Tsujii et al.

Claims 6-7, 9-21 and 55-62 are drawn to a method of obtaining a sample from a living mammal, such as urine, detecting/measuring an amount of PGH₂-EA metabolites, relating the amount measure to the activity of the COX-2 enzyme and/or relating the amount of the metabolites to a disease state or progression of a disease state, such as cancer/tumor, by comparing the activity of the COX-2 enzyme in the mammal with a standard value of a previously detected/measured amount, or further generating a standard curve.

Yu et al. (Reference BN: PTO-1449) teaches a method of detecting/measuring COX-2 from a mammalian cell, by detecting/measuring a PGH₂-EA metabolites (Figures 2-6 and pages 21182). Arachidonyl ethanolamide (AEA), a precursor for PGH₂-EA metabolites is not a substrate for COX-1 and therefore, the method of Yu et

al. only selectively detects COX-2 activity (page 21182, right column, page 21183, right column, page 21184, right column and page 21186, left column). Yu et al. teaches a method of detecting/measuring COX-2 activity by detecting PGH₂-EA metabolites via a mass chromatogram (Figures 3-5) and immunoassays (Figure 2 and Figure 6).

The difference between the reference of Yu et al. and the instant invention is that the reference of Yu et al. does not teach a method of detecting an activity of COX-2 enzyme in a living mammal by obtaining a sample from the living mammal, the step of comparing the detected amount of PGH₂-EA metabolite to a previously determined amount from the mammal (standard value)/generating a standard curve, step of relating the amount of the metabolites to a disease state or progression of a disease state, such as cancer/tumor, or by obtaining an urine sample from a mammal by comparing the activity of the COX-2 enzyme in the subject with a standard value of a previously detected/measured amount.

However, since Yu et al. teaches a method of only selectively detecting COX-2 activity in a sample, one having ordinary skill in the art would have concluded to apply the method of Yu et al. in detecting COX-2 activity from a sample obtained from a living mammal. Further, it is well established and known in the art that COX-2 expression is increased in cancerous cells, such as in colon cancer cells, as disclosed by Taketo et al. (reference BK: form PTO-1449). With this knowledge in hand, one having ordinary skill in the art would have concluded to apply the method of Yu et al. to relate the amount of PGH₂-EA metabolites and thereby COX-2 activity to disease state or progression of a disease state, such as colon cancer, by obtaining a sample from a

mammal, such as an urine or blood sample, and by comparing the activity of the COX-2 enzyme in the subject with a standard value of a previously detected/measured amount or a standard curve.

Therefore, combining the teachings of Yu et al. and Taketo et al., it would have been obvious to one having ordinary skill in the art to apply the method of Yu et al. in following the progression of colon cancer or to monitor colon cancer in a subject by detecting COX-2 activity in a mammal by obtaining a urine sample from said mammal and detecting PGH₂-EA metabolites and comparing the detected amount of PGH₂-EA metabolite to a previously determined amount from the mammal (standard value)/generating a standard curve. One of ordinary skill in the art would have been motivated to combine the references in order to follow the progression or monitor colon cancer in a subject by detecting COX-2 activity by detecting PGH₂-EA metabolites. One of ordinary skill in the art would have had a reasonable expectation of success since Yu et al. successfully teaches selective detection/measurement of COX-2 activity in a sample and Taketo et al. teaches that COX-2 expression and thereby activity of COX-2 is increased in colon cancer cells in subjects.

Therefore, the above references render claims 6-7, 9-21 and 55-62 *prima facie* obvious to one of ordinary skill in the art.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants should note that the rejection has been amended in light of the amendment of the claims.

Applicants argue that Yu et al. should be withdrawn as a primary reference because (1) Yu et al. does not relate to a living mammal and (2). Examiner respectfully disagrees. The instant rejection is not an anticipatory rejection, but an obviousness rejection. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The instant claims are not drawn to a method of detecting COX-2 activity directly in a mammal, but from a sample derived from a mammal by measuring PGH₂-EA metabolites. Said step of detecting COX-2 activity by detecting PGH₂-EA metabolites is taught by Yu et al. Therefore, Examiner takes the position that it would have been obvious to one having ordinary skill in the art to apply the teachings of Yu et al. to detect COX-2 activity in a mammal by obtaining a sample from said mammal and detecting PGH₂-EA metabolites.

Applicants also argue that Yu et al. is heading the opposite direction of the present invention because instead of taking a sample and then determining the presence of COX-2 activity, Yu et al. induces COX-2 activity and then determines if said induced COX-2 metabolizes AA and AEA. Examiner respectfully disagrees. Yu et al. does not teach away from the claimed invention. The crux of the reference of Yu et al. is that AA and AEA are metabolized by COX-2 but not COX-1. Therefore, it would have been obvious to one having ordinary skill in the art to apply the teachings of Yu et al. in determining COX-2 activity in a mammal (in following the progression of colon cancer or

to monitor colon cancer in a subject) by obtaining a sample from said mammal and compare the amount of PGH₂-EA metabolites in said sample.

Applicants also argue that the references cannot be combined because there is nothing in the reference associated with detecting an amount of a PGH₂-EA metabolite in the sample of a mammal. Examiner respectfully disagrees. As discussed above, the instant claims are not drawn to a method of detecting COX-2 activity directly in a mammal, but from a sample derived from a mammal by measuring PGH₂-EA metabolites. Said step of detecting COX-2 activity by detecting PGH₂-EA metabolites is taught by Yu et al. Therefore, Examiner takes the position that it would have been obvious to one having ordinary skill in the art to apply the teachings of Yu et al. to detect COX-2 activity in a mammal by obtaining a sample from said mammal and detecting PGH₂-EA metabolites.

Applicants also argue that Yu et al. does not teach a method of generating a standard value or curve for determining COX-2 activity. However, the instant rejection is an obviousness rejection. Generating a standard value or curve in measuring compound from a subject is routine in the art. In an effort of following the progression of a disease by detecting a PGH₂-EA metabolite, the step of comparing the detected amount of comparing the detected amount of PGH₂-EA metabolite to a previously determined amount from the mammal (standard value)/generating a standard curve to a previously determined amount from the mammal (standard value)/generating a standard curve would have been obvious and routine to one having ordinary skill in the art.

Hence the rejection is **maintained**.

Conclusion

None of the claims are in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/
Primary Examiner, Art Unit 1652